REMARKS

Claims 12-16, 19-20 and 23-24 remain pending in the application. Claim 23 has been cancelled. Accordingly, upon entry of this Amendment and Response, claims 12-16, 19-20 and 23 will be pending

The foregoing amendments have been made solely for the purpose of expediting prosecution of the present application and should in no way be construed as acquiescence to any of the Examiner's rejections. Applicants reserve the right to pursue the subject matter of the claims as originally filed or later amended in this or a separate application(s). No new matter has been added to the application.

Rejection of Claim 23 Under 35 USC § 112, First Paragraph

Claim 23 is rejected as failing to comply with the written description requirement. In particular, the Examiner is of the opinion that the phrase "therapeutic genes" is not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants respectfully traverse this rejection. However, in the interest of expediting prosecution, and in no way conceding to the rejection, claim 23 has been cancelled, rendering the rejection moot.

Rejection of Claim 23 Under 35 USC § 112, First Paragraph

Claim 23 is rejected as lacking enablement. In particular, the Examiner is of the opinion that the claimed formulation is not enabled with respect to antisense oligonucleotides, aptamers and therapeutic genes, because "those of ordinary skill in the art would not expect these [agents] to function properly since release outside the cell would trigger deactivation".

Applicants respectfully traverse this rejection. However, in the interest of expediting prosecution, and in no way conceding to the rejection, claim 23 has been cancelled, rendering the rejection moot.

Rejection of Claims 12-16, 19, 20, 23 and 24 Under 35 USC § 103(a)

Claims 12-16, 19, 20, 23 and 24 are rejected as being unpatentable over Kinstler *et al.* (referred to herein as Kinstler). In particular, the Examiner relies on column 19, lines 38-67, of

Kinstler as teaching N-terminal derivatization of interferon with polyethylene glycol, and column 11, lines 55-58 and 61 (incorporating by reference Remington's Pharmaceutical Sciences, (1990) 18th Ed pages 1475-1712) as teaching incorporation of said interferon derivatives into "particulate preparations" of polylactic acid and polyglycolic acid. The Examiner concludes that:

> "Those of ordinary skill would have found it well will to conjugate interferons or CSF with polyethylene glycol, and further to microencapsulate said conjugated bioactivities in a biodegradable polymer such as polylactic or polyglycolic acids, and further to expect similar therapeutic results from the use thereof given the teachings of Kinstler et al. The instant invention would have been obvious to one of ordinary skill at the time of invention given the teachings of Kinstler"

Applicants respectfully traverse this rejection for at least the following reasons:

I. Claims 12 and 13 of the of the present invention are drawn to a method for producing a pharmaceutical formulation for controlled release of an interferon by ***dissolving a biodegradable polymer and a conjugate of an interferon and a hydrophilic polymer in a solvent to form a monophase*** to form ***microparticles or nanoparticles*** comprising the biodegradable polymer encapsulating the conjugate.

The method taught by Kinstler involves N-terminal derivatization of interferon with polyethylene glycol and incorporation of the derivatized interferon into "particulate preparations of polymeric compounds such as polylactic acid and polyglycolic acid". This method does ***not*** involve dissolving the derivatized interferon and biodegradable polymer in a solvent to form a ***monophase***, nor does it involve formation of ***microparticles*** or ***nanoparticles***.

Remington, as incorporated by reference in Kinstler, fails to make up for this deficiency. This reference merely teaches general methods of microencapsulation in which thin coatings of materials (such as gelatin, polyvinyl alcohol, ethylcellulose, cellulose acetate phthalate or styrene anhydride) are applied to solid or liquid droplets to form a microcapsule. These methods do ***not*** involve dissolving the derivatized interferon and biodegradable polymer in a solvent to form a ***monophase***, nor does it involve formation of ***microparticles*** or ***nanoparticles***.

Neither Kinstler nor Remington, as referenced by Kinstler, teach or make obvious the presently claimed method for producing a pharmaceutical formulation which requires ***dissolving***

a biodegradable polymer and a conjugate of an interferon and a hydrophilic polymer in a solvent to form a monophase to form ***microparticles or nanoparticles*** comprising the biodegradable polymer encapsulating the conjugate. In fact, neither Kinstler nor Remington instruct the skilled artisan how to practice <u>any</u> method that involves forming a ***monophase*** of a biodegradable polymer and an interferon conjugated with a hydrophilic polymer. Nor has the Examiner provided any reason why one of ordinary skill would have been motivated to modify the teachings of Kinstler or Remington to arrive at the present invention (i.e., by forming a ***monophase*** of a biodegradable polymer and an interferon conjugated with a hydrophilic polymer).

II. Claims 14-16 are drawn to pharmaceutical formulations comprising a ***derivatized biodegradable polymer containing hydrophilic and hydrophobic regions***. Claims 19, 20 and 24 are drawn to pharmaceutical formulations comprising ***microparticles having a diameter predominantly between 20 and 100 um***.

As discussed above, Kinstler teaches N-terminal derivatization of interferon with polyethylene glycol and incorporation of the derivatized interferon into "particulate preparations of polymeric compounds such as polylactic acid and polyglycolic acid". Kinstler fails to teach or suggest pharmaceutical formulations comprising a ***derivatized biodegradable polymer containing hydrophilic and hydrophobic regions*** or ***microparticles with a diameter predominantly between 20 and 100 um***.

Remington, as incorporated by reference in Kinstler, fails to make up for this deficiency. As discussed above, Remington teaches general methods of microencapsulation in which thin coatings of materials (such as gelatin, polyvinyl alcohol, ethylcellulose, cellulose acetate phthalate or styrene anhydride) are applied to solid or liquid droplets to form a microcapsule. The microcapsules range in size from several "tenths of a μm to 5000μm". In contrast the presently claimed invention comprises ***microparticles*** with a diameter predominantly between ***20 and 100 um***. Remington fails to teach or render obvious a pharmaceutical formulation comprising a ***derivatized biodegradable polymer containing hydrophilic and hydrophobic regions***.

Accordingly, neither Kinstler nor Remington, as referenced by Kinstler, teach or suggest the presently claimed pharmaceutical formulations comprising a ***derivatized biodegradable polymer containing hydrophilic and hydrophobic regions*** or ***microparticles having a diameter***

predominantly between 20 and 100 um. Nor has the Examiner provided any reason why one of ordinary skill would have been motivated to modify the teachings of Kinstler to arrive at the present invention (i.e., by ***derivatizing a biodegradable polymer*** or producing ***microparticles with a diameter predominantly between 20 and 100 um***).

In summary, Kinstler and Remington fail to teach or suggest all the limitations of claims 12-16, 19, 20 and 24 of the present invention, even one had been motivated to combine these references as suggested by the Examiner. Moreover, even assuming, *in arguendo*, that all of the limitations of the present claims were disclosed by Kinstler and Remington (which they are not), the Examiner has not provided any reason why one of ordinary skill would have been motivated to modify the teachings of Kinstler and Remington to arrive at the presently claimed invention. Thus, the cited references fails to render claims 12-16, 19, 20 and 24 obvious under 35 USC §103 and Applicants respectfully request reconsideration and withdrawal of this rejection.

CONCLUSION

In view of the above amendment, Applicant believes the pending application is in condition for allowance.

Dated: June 26, 2007

Respectfully submitted,

By _____
Jane E. Remillard, Esq.
Registration No.: 38,872
LAHIVE & COCKFIELD, LLP
One Post Office Square
Boston, Massachusetts 02109-2127
(617) 227-7400
(617) 742-4214 (Fax)
Attorney/Agent For Applicant